

WHAT IS CLAIMED IS:

1. A method of making recombinant proteins using one or more apoptosis inhibitors, comprising the steps of:
  - (a) providing a vector comprising a gene encoding an apoptosis inhibitor,
  - (b) providing a vector comprising a gene encoding a protein of interest,
  - (c) providing a host cell,
  - (d) transforming or transfecting the host cell with the vector of steps (a) and (b),
  - (e) providing cell culture media,
  - (f) culturing the transformed or transfected host cell in the cell culture media under conditions sufficient for expression of the protein of interest and the apoptosis inhibitor, and optionally
  - (g) recovering or purifying the protein of interest from the host cell and/or the cell culture media.
2. The method of claim 1 further comprising the step of admixing an additional apoptosis inhibitor into the cell culture media in steps (e) or (f).
3. The method of claim 1 wherein the vector of step (a) and the vector of step (b) are the same vector.
4. The method of claim 1 wherein the vectors of steps (a) and (b) are two separate vectors.
5. The method of claim 4 wherein the vectors of steps (a) and (b) comprise different antibiotic resistance selection markers.
6. The method of claim 1 wherein the host cell is a CHO cell.
7. The method of claim 1 wherein the host cell is *E. coli*.
8. The method of claim 1 wherein the apoptosis inhibitor gene of step (a) encodes for the caspase-9 dominant negative protein or baculovirus p35.
9. The method of claim 1 wherein the host cells are cultured under conditions for transient expression of the protein of interest.

10. The method of claim 1 wherein the protein of interest comprises a protein which is capable of inducing apoptosis in a mammalian or non-mammalian cell.

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11. The method of claim 1 wherein said cell culture media is serum-free media.

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12. The method of claim 1 wherein said cell culture media comprises butyrate.

13. The method of claim 1 wherein after step (f), the host cell(s) and/or cell culture media is frozen and subsequently thawed.

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14. A method of making recombinant proteins using one or more apoptosis inhibitors, comprising the steps of:

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(a) providing a vector comprising a gene encoding a protein of interest,

(b) providing a host cell comprising a gene encoding an apoptosis inhibitor,

(c) transforming or transfecting the host cell with the vector of step (a),

(d) providing cell culture media,

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(e) culturing the transformed or transfected host cell in the cell culture media under conditions sufficient for expression of the protein of interest and the apoptosis inhibitor, and optionally

(f) recovering or purifying the protein of interest from the host cell and/or cell culture media.

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15. The method of claim 14 wherein the gene encoding the apoptosis inhibitor is stably integrated into the genome of the host cell.

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16. The method of claim 14 further comprising the step of admixing an additional apoptosis inhibitor molecule into the cell culture media in steps (d) or (e).

17. The method of claim 14 wherein the host cell is a CHO cell.

18. The method of claim 14 wherein the host cell is *E. coli*.

19. The method of claim 14 wherein the apoptosis inhibitor gene of step (b) encodes for the caspase-9 dominant negative protein or baculovirus p35.
- 5 20. The method of claim 14 wherein said cell culture media comprises butyrate.
21. The method of claim 14 wherein after step (e), the host cell(s) and/or cell culture media is frozen and subsequently thawed.
- 10 22. A method of making recombinant proteins using one or more apoptosis inhibitors, comprising the steps of:
- a) providing a vector comprising a gene encoding a protein of interest,
  - 15 b) providing a host cell,
  - c) transforming or transfecting the host cell with the vector of step (a),
  - d) providing cell culture media,
  - e) providing an apoptosis inhibitor,
  - 20 f) admixing the apoptosis inhibitor into the cell culture media,
  - g) culturing the host cell in the cell culture media under conditions sufficient for expression of the protein of interest, and optionally
  - h) recovering or purifying the protein of interest from the host cell and/or the cell culture media.
- 25 23. The method of claim 22 wherein the host cell is a CHO cell.
24. The method of claim 22 wherein the apoptosis inhibitor comprises an organic or inorganic molecule.
- 30 25. The method of claim 24 wherein the apoptosis inhibitor comprises z-VAD-fmk.
- 35 26. The method of claim 22 wherein after step (g), the host cell(s) and/or cell culture media is frozen and subsequently thawed.
27. A method of increasing yield of a protein of interest in a cell culture, comprising the steps of:

(a) providing a vector comprising a gene encoding an apoptosis inhibitor selected from the group consisting of caspase-9 dominant negative protein and baculovirus p35,

5 (b) providing a vector comprising a gene encoding a protein of interest,

(c) providing a host cell,

(d) transforming or transfecting the host cell with the vector of steps (a) and (b),

(e) providing cell culture media,

10 (f) culturing the transformed or transfected host cell in the cell culture media under conditions sufficient for expression of the protein of interest and an amount of the apoptosis inhibitor which is effective in increasing yield of the protein of interest, and optionally

15 (g) recovering or purifying the protein of interest from the host cell and/or the cell culture media.

28. The method of claim 27 wherein said host cell is a CHO cell,

20 29. The method of claim 27 wherein said cell culture media is serum-free media.

30. The method of claim 27 wherein after step (f), the host cell(s) and/or cell culture media is frozen and subsequently thawed.

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31. A method of prolonging host cell viability in a cell culture, comprising the steps of:

30 (a) providing a vector comprising a gene encoding an apoptosis inhibitor selected from the group consisting of caspase-9 dominant negative protein and baculovirus p35,

(b) providing a vector comprising a gene encoding a protein of interest,

(c) providing a host cell,

35 (d) transforming or transfecting the host cell with the vector of steps (a) and (b),

(e) providing cell culture media,

(f) culturing the transformed or transfected host cell in the cell culture media under conditions sufficient for expression of the protein of

interest and an amount of the apoptosis inhibitor which is effective for prolonging viability of the host cells in the cell culture, and optionally

(g) recovering or purifying the protein of interest from the host cell and/or the cell culture media.

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32. The method of claim 31 wherein the vector comprising the gene encoding the apoptosis inhibitor includes an inducible promoter.

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33. A composition of matter comprising a protein of interest produced in accordance with the method of claim 1.

34. A composition of matter comprising a protein of interest produced in accordance with the method of claim 14.

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35. A composition of matter comprising a protein of interest produced in accordance with the method of claim 22.

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36. A composition of matter comprising a protein of interest produced in accordance with the method of claim 27.

37. A composition of matter comprising a protein of interest produced in accordance with the method of claim 31.